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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/502,945	02/11/00	SCANLAN	M L0461/7081-(

HM12/0717

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EXAMINER	
DAVIS,N	
ART UNIT	PAPER NUMBER
1642	9

DATE MAILED: 07/17/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/502,945	Applicant(s) SCANLAN ET AL.	
	Examiner Natalie A. Davis	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *11 May 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,37-40,58,63 and 67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,37-40,58,63 and 67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election of SEQ ID NO: 2 in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Claims 6, 37-40, 58, 63, and 67 are pending and examined on the merits to the extent that they read on the elected species, SEQ ID NO: 2.

Priority

2. This application filed under former 37 CFR 1.60 lacks the necessary reference to the prior application. A statement reading "This is a divisional of Application No. 08/948,705, filed 10/10/97." should be entered following the title of the invention or as the first sentence of the specification. Also, the current status of all nonprovisional parent applications referenced should be included.

Specification

3. The disclosure is objected to because of the following informalities: The preliminary amendment, paper number 2, dated 11 Feb 2000, amended page 4. The amendment requested: "On page 4, lines 13-14, please delete '08/580,980, and Application Serial No. 08/479,328, filed on Jun 7, 1995 and January 3, 1996, respectively' and insert -5,698,396-therefor." As a result of the amendment, only one patent is referenced in the specification. Applicant is required to either add a second document number or refer back to the document in the singular rather than the plural.

Claim Rejections - 35 USC § 112

4. Claims 6, 37-40, 58, 63, and 67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The claims are drawn to proteins encoded by nucleic acid molecules which encode a cancer associated antigen, and which comprise a nucleotide sequence, the complementary sequence of which hybridizes, under stringent conditions, to the nucleotide sequence as set forth as SEQ ID NO: 2, the isolated protein encoded by the nucleotide sequence as set forth as SEQ ID NO: 2, or the composition of matter useful in stimulating an immune response to the protein encoded by the nucleotide sequence as set forth SEQ ID NO: 2. Sahin et al. "Human neoplasms elicit multiple specific immune responses in the autologous host" Proc. Natl. Acad. Sci., Vol. 92, pp. 11810-11813, December 1995, teaches that (page 11810, first paragraph), "A prerequisite for the successful application of recombinant tumor vaccines and

other immunotherapeutic interventions in cancer patients is the recognition by the immune system of tumor-specific and tumor-associated antigens (i.e., of molecules that are overexpressed or specifically expressed in the tumor cells). Despite the extensive efforts that have been made in recent years to identify such tumor antigens in human neoplasms, to date only a few have been defined at the molecular level."

The specification does not teach that the polynucleotide sequences of SEQ ID NO:3 and 4 are actually translated into protein which is expressed in any disease state. Although the specification teaches that HIBP mRNA is expressed in tissue libraries associated with cell proliferation, inflammation and immune response there is no objective evidence that SEQ ID NO:3 and 4 is translated to SEQ ID NO:1 and 2. Those of skill in the art, recognize that expression of mRNA does not dictate the translation of such mRNA into a polypeptide. For example, Alberts et al. (Molecular Biology of the Cell, 3rd edition, 1994, page 465) teach that translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferrin receptor polypeptide is translated. Many other proteins are regulated at the translational level rather than the transcriptional level. Thus, predictability of protein translation is not necessarily contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation.

The disclosure teaches the nucleotide sequences as set forth in SEQ ID NOs: 1-8, can be exploited for (page 2, lines 1-3), diagnosing and treating colon cancer. However, the specification teaches that the SEQ ID NOs: 1 and 2 were found to be amplified in all tissues tested (page 10, line 3), as were SEQ ID NOs: 4 and 5 (page 10, line 18), which included (page 9, lines 12-14) lung, testis, small intestine, colon, breast, liver and placenta tissues from normal samples, and a colon tumor sample. The working examples do not clearly show that the claimed peptides are in fact actually cancer associated antigens and if they are actually translated into proteins, as only mRNA expression was detected.

Absent evidence that the disclosed sequences are overexpressed or specifically expressed in colon cancer cells, and absent evidence that encoded proteins (if encoded) would effectively induce MHC restricted T cell responses, one of skill in the art would not be able to practice the claimed invention without undue experimentation.

5. Claims 37-40, 63 and 67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are drawn to a composition of matter comprising the peptides, which bind to one or more MHC molecules presented on the surface of cells expressing an abnormal amount of the protein, and elicit a cytolytic response thereto. Greenberg et al., U. S. Patent 5,470,730, teach (column 15) the that "a major goal of tumor therapy is to transfer tumor-specific MHC restricted T cells similar to the MHC restricted HIV-specific T cells, but the clinical trials thus far have frequently used non-MII C restricted populations of cytolytic effector cells, in part due to the difficulties identifying human tumor antigens that will effectively induce MHC restricted T cell responses."

The specification does not provide any description regarding the proteins encoded by the nucleic acids, either by their amino acid sequence or their common structural features, and does not disclose the properties of the proteins, including the binding of peptides, encoded by the nucleotide sequences set forth as SEQ ID NOs: 1-5, to MHC molecules. There is no guidance as to how to induce a T-cell immune response using the claimed peptides. There are no working examples describing effective inducement of MHC restricted T-cell responses. Therefore, absent such teachings, one of skill in the art would not be able to practice the claimed invention because undue experimentation would be required.

6. Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a "written description rejection, based upon the revised Interim Written Description guidelines published in the Federal Register (Volume 63, Number 114, pages 32639-32645) on December 21, 1999.

Claim 6 is drawn to nucleic acid molecule which encode a cancer associated antigen, and which comprises a nucleotide sequence, the complementary sequence of which hybridizes, under stringent conditions, to at least one second nucleic acid molecule

comprising a nucleotide sequence selected from the group consisting of the nucleotide sequences set forth as SEQ ID NO: 2, nucleic acid molecules that differ from the nucleic acid molecules above in codon sequence due to the degeneracy of the genetic code, and complements of the two types of nucleic acids. The claim is broad and not commensurate in scope with that which is described in the specification. An inordinate number of species read on the claim, as no length is given to the nucleic acid molecule which hybridize to the sequence as set forth as SEQ ID NO: 2. The specification discloses nucleic acid sequences set forth as SEQ ID NO: 1, 2, 3, 4, and 5, and isoforms of SEQ ID NOS: 1 and 4, set forth as SEQ ID NOS: 6, 7, and 8. The disclosure of one or two species may provide an adequate written description of a genus when the speices disclosed are representative of the genus; the specification discloses full length nucleic acid sequences associated with colon cancer; however, it does not teach the common structure or features of colon cancer related proteins. Absent such disclosure, the structures of the disclosed nucleic acid sequences are not sufficiently descriptive of a representative number of species encompassed by the genus to sufficiently describe the genus as a whole. One of skill in the art would not be able to envision the structure of other colon cancer related nucleic acids. Furthermore, the specification does not describe species of proteins, either by amino acid sequence or by common structural features. Therefore, the specification does not describe the claimed genus in such full, clear, concise and exact terms to indicate that applicants had possession of the genus at the time of filing of the present application.

7. Claims 6 and 38-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 6 is drawn to complements of nucleic acids, which encode a cancer associated antigen. Claim 6 is indefinite because the size of the complements are unclear. It is not clear whether these are full sized complements, partial, or both. The disclosure fails to teach the metes and bounds of "complements".

Claim Rejections - 35 USC § 101

8. Claims 6, 37-40, 58, 63, and 67 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The Revised Interim Utility Guidelines require disclosure of at least one specific and substantial, and credible utility for an invention, or for the invention to have a well-established utility that is specific, substantial, and credible. The disclosure teaches the nucleotide sequences as set forth in SEQ ID NOs: 1-8. The disclosure makes a general statement that the invention is drawn to genes associated with colon cancer and makes general statements regarding "diagnostic markers" and antibody production (page 1, lines 1-14). However, the specification fails to assert any specific and substantial utility for the claimed peptides and proteins. Furthermore, the specification fails to disclose a credible utility for the claimed proteins or peptides associated with colon cancer by teaching that the SEQ ID NOs: 1 and 2 were found to be amplified in all tissues tested (page 10, line 3), as were SEQ ID NOs: 4 and 5 (page 10, line 18), which included (page 9, lines 12-14) lung, testis, small intestine, colon, breast, liver and placenta tissues from normal samples, and a colon tumor sample. Sahin et al. "Human neoplasms elicit multiple specific immune responses in the autologous host" Proc. Natl. Acad. Sci., Vol. 92, pp. 11810-11813, December 1995, teaches that (page 11810, first paragraph), "A prerequisite for the successful application of recombinant tumor vaccines and other immunotherapeutic interventions in cancer patients is the recognition by the immune system of tumor-specific and tumor-associated antigens (i.e., of molecules that are overexpressed or specifically expressed in the tumor cells). Despite the extensive efforts that have been made in recent years to identify such tumor antigens in human neoplasms, to date only few have been defined at the molecular level. Absent evidence that the disclosed sequences are overexpressed or specifically expressed in colon cancer cells, the invention does not have a specific, substantial, and credible utility.

Claims 6, 37-40, 58, 63, and 67 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Natalie A. Davis whose telephone number is 703-308-6410. The examiner can normally be reached on M-F 8-5:30 (every other Friday off).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4315 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Natalie A. Davis, Ph.D.
July 13, 2001

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